### PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY			REC'D 17 MAY	2035
To:		PCT	\:\":-O	P
J. PETER FASSE				
FISH & RICHARDSON, P.C. 225 FRANKLIN STREET	WRI	TTEN OPINION	OF THE	
BOSTON, MA 02110-2804	INTERNATIO	NAL SEARCHIN	G AUTHORITY	
		(PCT Rule 43bis.	1)	<b>-</b>
	Date of mailing (day/month/year)	12 MAY	2005	_ ·
Applicant's or agent's file reference	FOR FURTHER	ACTION See paragraph 2 below	<b>,</b>	
00786-607WO1  International filing date	(day/month/year)	Priority date (day/mo	onth/year)	
international approaches to		30 January 2004 (30	.01.2004)	
PCT/US05/03158 31 January 2005 (31.01 International Patent Classification (IPC) or both national classification	ation and IPC	30 January 300 (		1
International Patent Classification (IPC) of both into all the	505/160 187 307 3	540	·	
IPC(7): C08F 120/32, 283/10; C08L 71/02, 79/02 and US Cl.:	323/102, 107, 327. 3			
Applicant	•			
THE GENERAL HOSPITAL CORPORATION				
1. This opinion contains indications relating to the following ite	ems:			
Box No. I Basis of the opinion		••		
Box No. II Priority				1
Box No. III Non-establishment of opinion with	regard to novelty, inv	entive step and indust	trial applicability	
Box No. IV Lack of unity of invention				
Box No. V Reasoned statement under Rule 43/ applicability; citations and explana	bis.1(a)(i) with regard	to novelty, inventive statement	step or mousural	
Box No. VI Certain documents cited				
Box No. VII Certain defects in the international	l application			
Box No. VIII Certain observations on the interns				
	٠.			<u> </u>
2. FURTHER ACTION  If a demand for international preliminary examination is a demand for international preliminary examination is a second control of the co	made, this opinion w	ill be considered to be	e a written opinion of the	ie an
If a demand for international preliminary examination is a International Preliminary Examining Authority ("IPEA"). Authority other than this one to be the IPEA and the chose that the chose is a second of the IPEA and the chose is a second of the IPEA.	) except that this do sen IPEA has notified	the International Bure	eau under Rule 66.1bis	b)
Authority other than this one to be the IPEA and the chost that written opinions of this International Searching Authority				
If this opinion is, as provided above, considered to be a	written opinion of the	PEA, the applicant the expiration of 3	is invited to submit to the months from the date	he of
mailing of Form PCT/ISA/220 or before the expiration of	22 months from the	priority date, whichever	er expires later.	
For further options, see Form PCT/ISA/220.				ļ
3. For further details, see notes to Form PCT/ISA/220.				
Name and mailing address of the ISA/ US	Authorized of	ficer	1	
Mail Stop PCT, Atm: ISA/US	James Seidle	eck	lean Proctor	
Commissioner for Patents P.O. Box 1450		702 202 0661	Party Paralogal Sin	-
Alexandria, Virginia 22313-1450	Telephone No	o. 703-308-0661		

Facsimile No. (703) 305-3230
Form PCT/ISA/237 (cover sheet) (January 2004)

International application No.
PCT/US05/03158

Box No. I Basis of this opinion	╝
1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.	h.
This opinion has been established on the basis of a translation from the original language into the following language which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).	•
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:	
a. type of material	
a sequence listing	
table(s) related to the sequence listing	
b. format of material	
in written format	
in computer readable form	
c. time of filing/furnishing	
contained in international application as filed.	
filed together with the international application in computer readable form.	
furnished subsequently to this Authority for the purposes of search.	
· · ·	
In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.	l 1
4. Additional comments:	
	•
$\cdot$	
$\boldsymbol{\cdot}$	
•	

International application No. PCT/US05/03158

Box No. V	Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial
	applicability; citations and explanations supporting such statement

#### 1. Statement

Novelty (N)	Claims 4-9, 12, 14-36	YES
	Claims <u>1-3, 10-11, 13</u>	NO
Inventive step (IS)	Claims 4-9, 12, 14-36	YES
	Claims 1-3, 10-11, 13	NO
Industrial applicability (IA)	Claims 1-36	YES
	Claims NONE	NO

#### 2. Citations and explanations:

Claims 1-3, 10-11, 13 lack novelty under PCT Article 33(2) as being anticipated by RANGER et al U.S. Patent 6,780,428.

RANGER discloses star-shape polymers having an inner core and an outer shell. The inner core comprises a hydrophobic vinyl compound such as (alkyl)acrylate and (alkyl)acrylamide and derivatives. The outer shell is obtained from the polymerization of hydrophilic vinyl compounds including a vinyl terminated polyethylene glycol, N-vinyl-2-pyrrolidone, N-isopropyl acrylamide and their related derivatives, column 5, lines 19-39. Claimed hyperbranched polymer having core/shell structure and having an active hydrogen-containing group on the outer shell segment is readable in RANGER's invention.

Claims 1-3 and 13 lack novelty under PCT Article 33(2) as being anticipated by KABANOV et al U.S. Patent 6,440,743.

KABANOV discloses star block copolymer having more than two polymer segments linked to a single center, col. 3, lines 45-60 and col. 4, lines 1-5. The star polymer can be used in Gene therapy, col. 10, lines 58-60 and col. 11, lines 34-67. The diamine-linked pluronic copolymer of formula (XVII), column 13, lines 40-55 and col. 14, lines 21-30 is readable in applicants' claims.

Claims 1-3 lack novelty under PCT Article 33(2) as being anticipated by YOUNGS et al U.S. Patent 6,288,197.

YOUNGS discloses dendrimer copolymer comprising a core segment and the dendritic branches with terminal NH2 groups, Figure 1, col. 4, lines 24-67, col. 5, line 33 and column 15, lines 42-54.

Claims 4-9, 12, 14-36 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a hyperbranched polymer having core-shell structure wherein an inner core comprises a network of covalently bound molecular chains comprising ether linkage, the two heteroatoms are each oxygen atoms, the two oxygen atoms are spaced apart by at least four atoms.

Claims 1-36 meet the criteria set out in PCT Article 33(4), and thus has industrial applicability because the subject matter claimed can be made or used in industry.

## PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY	·		REC'D 1/MAY	2035
To:		PCT	\\('\\\'\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	P
J. PETER FASSE FISH & RICHARDSON, P.C. 225 FRANKLIN STREET BOSTON, MA 02110-2804	WRI	TTEN OPINION ( )NAL SEARCHIN	OF THE IG AUTHORITY	
-		(PCT Rule 43bis.		7
	Date of mailing (day/month/year)	12 MAY	2005	-
Applicant's or agent's file reference	FOR FURTHER	See paragraph 2 below	•	
00786-607WO1	(downwanth higgs)	Priority date (day/mo	onth/year)	1
International application No. International fulling date				
PCT/US05/03158 31 January 2005 (31.01	1.2005)	30 January 2004 (30	.01.2004)	
International Patent Classification (IPC) or both national classific	andii am n C	540		
IPC(7): C08F 120/32, 283/10; C08L 71/02, 79/02 and US Cl.:	525/162, 187, 327. 3	, 540		
Applicant				
THE GENERAL HOSPITAL CORPORATION				
indications relating to the following its	ems:	•		l
1. This opinion contains indications relating to the following its				
Box No. I Basis of the opinion				
Box No. II Priority		·	-ial applicability	
Box No. III Non-establishment of opinion with	regard to novelty, inv	ventive step and indust	Ital applications	
Box No. IV Lack of unity of invention			. Ainl	
Box No. V Reasoned statement under Rule 43 applicability; citations and explana	bis.1(a)(i) with regardations supporting such	I to novelty, inventive statement	step or industrial	
Box No. VI Certain documents cited				
Box No. VII Certain defects in the international	l application			
Box No. VIII Certain observations on the intern	ational application			
2. FURTHER ACTION  If a demand for international preliminary examination is a International Preliminary Examining Authority ("IPEA" Authority other than this one to be the IPEA and the chost that written opinions of this International Searching Authority	en IPEA has notified	the International Bure	e a written opinion of the applicant chooses a cau under Rule 66.1 bis (	ne an b)
If this opinion is, as provided above, considered to be a IPEA a written reply together, where appropriate, with mailing of Form PCT/ISA/220 or before the expiration of	written opinion of the	PEA, the applicant	is invited to submit to the months from the date	he
For further options, see Form PCT/ISA/220.				
3. For further details, see notes to Form PCT/ISA/220.		· · · · · · · · · · · · · · · · · · ·		
Name and mailing address of the ISA/ US	Authorized of		- 1	
Mail Stop PCT, Attn: ISA/US  Commissioner for Patents  P.O. Box 1450	James Seidle Telephone No	ck 5. 703-308-0661	Person Proctor Person Paralogal Sec	-
Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230				

Form PCT/ISA/237 (cover sheet) (January 2004)

International application No.
PCT/US05/03158

Box No	o. I Basis of this opinion	•
1. With it was	regard to the language, this opinion has been established, unless otherwise indicated under this item.	ed on the basis of the international application in the language in which
	This opinion has been established on the basis of a translation furnished for the	nslation from the original language into the following language e purposes of international search (under Rules 12.3 and 23.1(b)).
2. With claim	regard to any nucleotide and/or amino acid seque ed invention, this opinion has been established on the b	nce disclosed in the international application and necessary to the asis of:
a.	type of material	
	a sequence listing	
	table(s) related to the sequence listing	
b.	format of material .	
	in written format	
	in computer readable form	
c.	time of filing/furnishing	
	contained in international application as filed.	•
	filed together with the international application	in computer readable form.
	furnished subsequently to this Authority for the	purposes of search.
·		
3.	In addition, in the case that more than one version filed or furnished, the required statements that the in the application as filed or does not go beyond the app	or copy of a sequence listing and/or table relating thereto has been aformation in the subsequent or additional copies is identical to that in plication as filed, as appropriate, were furnished.
4. Addi	tional comments:	•
		• •
	•	•
	•	
•		

International application No. PCT/US05/03158

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

#### 1. Statement

Novelty (N)	Claims 4-9, 12, 14-36	YES
	Claims 1-3, 10-11, 13	NO
	Claima 4.0 12 14.26	YES
Inventive step (IS)	Claims 4-9, 12, 14-36	
	Claims 1-3, 10-11, 13	NO
		YES
Industrial applicability (IA)	Claims <u>1-36</u>	<del></del> <del></del>
•	Claims NONE	NO

#### 2. Citations and explanations:

Claims 1-3, 10-11, 13 lack novelty under PCT Article 33(2) as being anticipated by RANGER et al U.S. Patent 6,780,428.

RANGER discloses star-shape polymers having an inner core and an outer shell. The inner core comprises a hydrophobic vinyl compound such as (alkyl)acrylate and (alkyl)acrylamide and derivatives. The outer shell is obtained from the polymerization of hydrophilic vinyl compounds including a vinyl terminated polyethylene glycol, N-vinyl-2-pyrrolidone, N-isopropyl acrylamide and their related derivatives, column 5, lines 19-39. Claimed hyperbranched polymer having core/shell structure and having an active hydrogen-containing group on the outer shell segment is readable in RANGER's invention.

Claims 1-3 and 13 lack novelty under PCT Article 33(2) as being anticipated by KABANOV et al U.S. Patent 6,440,743.

KABANOV discloses star block copolymer having more than two polymer segments linked to a single center, col. 3, lines 45-60 and col. 4, lines 1-5. The star polymer can be used in Gene therapy, col. 10, lines 58-60 and col. 11, lines 34-67. The diamine-linked pluronic copolymer of formula (XVII), column 13, lines 40-55 and col. 14, lines 21-30 is readable in applicants' claims.

Claims 1-3 lack novelty under PCT Article 33(2) as being anticipated by YOUNGS et al U.S. Patent 6,288,197.

YOUNGS discloses dendrimer copolymer comprising a core segment and the dendritic branches with terminal NH2 groups, Figure 1, col. 4, lines 24-67, col. 5, line 33 and column 15, lines 42-54.

Claims 4-9, 12, 14-36 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a hyperbranched polymer having core-shell structure wherein an inner core comprises a network of covalently bound molecular chains comprising ether linkage, the two heteroatoms are each oxygen atoms, the two oxygen atoms are spaced apart by at least four atoms.

Claims 1-36 meet the criteria set out in PCT Article 33(4), and thus has industrial applicability because the subject matter claimed can be made or used in industry.